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(71)(72) Applicant and Inventor: SHIU, Man, Fai [GB/GB]; Cardiovascular Innovations Consultancy, 39 Dyott Road, Moseley, Birmingham B13 9QZ (GB).

(74) Agent: HEALY, Cecilia, Patricia; E.N. Lewis & Taylor, 5 The Quadrant, Coventry CV1 2EL (GB).

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(57) Abstract

A catheter (22, 28) comprises a hollow lumen having a distal end provided with a tip (23, 39) for insertion into a blood vessel, a plurality of peripherally spaced holes (27, 38) closely adjacent the tip (23, 39), the tip having a terminal aperture (25, 40) capable of adopting two configurations, namely an enlarged wire carrying configuration in which it is capable of receiving and passing a wire (24, 34), and a restricted configuration in which it is of substantially smaller cross-sectional area than in the enlarged condition, the aperture (25, 40) being normally biased into said restricted configuration. The aperture (25, 40) may comprise a slit or a plurality of slits (26) or a peripheral restrictor (31, 33) in the form of an annulus or a plurality of restrictor members of resilient material such as latex or silicone rubber. The catheter, intended for use in blood vessels, may find uses in coronary work, for example coronary angiography or interventional procedures such as balloon angioplasty or the insertion of stents, as well as for other arterial work.

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CATHETER

This invention relates to a catheter intended primarily for contrast angiography and interventional procedures. It was devised with a view to improving safety and efficacy in procedures in the coronary arteries but may have application in all arterial work such as neuro-radiology and peripheral arterial work. It is to be understood that the present invention does not relate to all forms of medical catheters, for example urological catheters, but only to those for use in blood vessels.

Conventional blood vessel catheters fall into various types. Firstly, some have an end hole but no other apertures, for example the Judkins type which takes both left and right hand forms for investigation of the left and right coronary arteries; others have side holes only, for example the NIH catheter. A third type exemplified by the Gensini catheter have an end hole and a number of side holes.

Although present conventional catheters are successfully used in many cases, each design has disadvantages which may give rise to serious complications in a small but significant number of patients.

Considering the first mentioned type of catheter, having an end hole only, this enables an introducing wire to be used, having an atraumatic tip, which is positioned in the region of the coronary artery or other artery to be investigated. The catheter is manoeuvred into position on the wire and then the wire is removed, leaving the catheter in position.

The wire is soft tipped often with a small curved tip to reduce trauma during catheter advance and positioning. This allows preliminary exploration of curved and diseased arteries

for example. The wire also serves the function for example with the pre-formed shaped Judkins catheter of straightening out the catheter as it is passed into position. Finally, the use of a wire allows the exchange of catheters without the loss of access to the same artery or arterial segment.

Where an introducing wire cannot be used, these advantages are lost. Thus, catheters of the second type referred to above, having side holes only, lose the advantages of accommodating the introducing wire.

However the first type of catheter, having an end hole, does have certain disadvantages. The end hole tends to have a sharp edge which can injure the walls of the blood vessel during positioning of the catheter. Where contrast angiography is carried out, the forceful injection of contrast medium may also have a traumatic effect on the vessel wall because the contrast medium emerges as a single forwardly directed forceful jet. In a small number of cases, perhaps 0.3%, dissection of the arterial wall can occur, with serious risk to the patient.

Imaging can also be defective as the contrast medium can tend to issue in a stream along the lumen of the artery, giving an indistinct image of the vessel wall. If the artery branches, the injected medium may subselect one of two or three branches, giving poor or indeed no imaging of the other branches.

It may sometimes be an advantage that a single end hole allows precise position for pressure measurements and in certain circumstances, precise injection of contrast, although the need for the latter is rare. Conversely, however, if the single end hole is positioned in abutment with an arterial wall, pressure monitoring ceases and injection of contrast medium can prove dangerous.

Catheters of the second type, having side holes only, are recognised to have a higher degree of safety because there is no sharp tip and they are therefore less traumatic during manoeuvring. Injection of contrast medium through the catheter gives better imaging because the contrast medium sprays laterally outwardly from the catheter, showing the contours of the arterial wall and picking up any local side branches. There is also less tendency for the side hole only catheter to recoil from its chosen position during injection. However such catheters have the major disadvantage that they cannot be deployed over a wire and need other techniques, for example the use of a guide catheter or sheath to position them.

Where both end hole and side holes are provided, as in the known Gensini catheter, a positioning wire can be used and some of the advantages of side holes are provided. However, there is still the problem of the risk of trauma from the apertured tip.

It is an object of the present invention to provide a new or improved catheter primarily for contrast angiography and interventional procedures in blood vessels.

According to the invention there is provided a catheter having a hollow lumen having a distal end provided with a tip for insertion into a blood vessel, a plurality of peripherally spaced holes closely adjacent the tip, the tip having a terminal aperture capable of adopting two configurations, namely an enlarged wire carrying configuration in which it is capable of receiving and passing a wire, and a restricted configuration in which it is of substantially smaller cross-sectional area than in the enlarged condition, the aperture being normally biased into said restricted configuration.

The terminal aperture may comprise a slit or a plurality of

intersecting slits. Alternatively, the aperture may be provided with a resilient peripheral restrictor which may comprise an annulus of resilient material surrounding and at least partly closing the aperture or which may comprise a plurality of inwardly projecting resilient restrictor members which at least partly close the aperture.

The resilient peripheral restrictor may comprise latex or silicone rubber.

The catheter may be coated with the same material as forms the resilient peripheral restrictor.

In an alternative, the aperture may comprise a valve openable by a wire.

The catheter may comprise a diagnostic coronary angiogram catheter or may comprise a guiding catheter for interventional procedures such as PTCA.

Embodiments of the invention will now be described in more detail by way of example only, with reference to the accompanying drawings, in which:-

Figure 1 shows a prior art catheter tip having a terminal aperture,

Figure 2 shows a prior art catheter tip having side apertures but no terminal aperture,

Figure 3A shows a prior art catheter tip having a terminal aperture and side apertures at a distance from the tip,

Figure 3B shows a prior art catheter similar to that in Figure 3A but with side apertures close to the tip,

Figure 4 shows a prior art Judkins type catheter having a terminal aperture,

Figure 5 shows the present invention applied to a Judkins type catheter,

Figure 6 is an enlarged detail view of the tip of the catheter shown in Figure 5 with a tip aperture in a restricted configuration,

Figure 6A is a detail end view of the tip shown in Figure 6,

Figure 7 shows the catheter of Figure 5 with the tip aperture in an enlarged wire carrying configuration,

Figure 8 illustrates an alternative form of tip in cross-section in the normal restricted configuration,

Figure 8A is a detail end view of the tip shown in Figure 8,

Figure 8B is a detail end view of a still further alternative of the tip shown in Figure 8,

Figure 9 illustrates the tip of Figure 8 in the enlarged wire carrying configuration,

Figure 10 illustrates the catheter tip of Figures 8 and 9 in use during contrast angiography, illustrating ease of visualisation of small side branches.

Referring firstly to the generalised diagrammatic illustrations forming Figures 1 to 3, Figure 1 shows the tip 10 of a catheter having an end hole 11 which is of the same internal diameter as the lumen of the catheter. This is a type of catheter exemplified by the Judkins left and right catheters such as that illustrated in Figure 4. As previously

referred to, this type of catheter can be used in combination with an introducing or guide wire by well known techniques. The use of the guide wire enables it to be positioned accurately. However the tip aperture 11 has a relatively sharp edge which may cause trauma. This problem is addressed particularly in larger sizes of catheter by the use of a "soft tip" in which the catheter is coated with a latex or silicone rubber material over a relatively firm core, the latex or silicone material extending beyond the firm core at the tip to provide a so called "soft tip". However there is no change in the internal diameter of the catheter at the tip.

Figure 2 shows diagrammatically a form of catheter 13 which has a closed end 14 which is of rounded configuration. This catheter has a plurality of side holes 15 arranged peripherally near to the tip 14.

It cannot be positioned using a guide wire and therefore a different introducing technique needs to be used. For example it may be introduced along a pre-positioned guide catheter of larger size which needs then to be removed or to be inserted via a shorter, but possibly less advantageous arterial route.

The NIH catheter is a typical example of the type of catheter shown in Figure 2.

The third form of prior art catheter is illustrated in Figures 3A and 3B comprises a catheter 16 having an end hole 17 similar to the end hole 11 of Figure 1 and also has a plurality of side holes 18 which, however, are either spaced by a distance of perhaps 2 cm to 3 cm from the distal tip and the end hole 17 (Figure 3A) or close to the tip (Figure 3B).

A wire can be used for positioning the catheter.

Turning to Figure 4 of the drawings, this shows a prior art

left coronary Judkins catheter 20 having a single end hole 21.

In Figure 5, a catheter embodying the present invention has been illustrated at 22 and an enlarged view of the distal tip portion 23 is shown in Figure 6.

The extreme free end of the tip portion 23 has a terminal aperture in the form of three slits meeting at a point as shown in Figure 6A. This construction is by way of example and it would be possible to provide more or fewer slits or even a single slit provided that the aperture is capable of adopting two configurations.

In the configuration shown in Figures 6 and 6A, the actual aperture has a very small cross-sectional area and this is the normal condition. In other words, the aperture is biased into this restricted configuration. This may be a result of the nature of the materials of which the catheter is made or of some mechanical constraint.

In Figure 7, the catheter of Figures 5 and 6 is shown in an alternative configuration.

A guide wire 24 has been passed into a suitable position in a blood vessel and the catheter 22 has been slid along the guide wire until it is in its correctly deployed condition. The tip 23 has its aperture 25 opened up so that each of the slits 26 spreads apart and the effective cross-sectional area of the aperture is enlarged.

When the catheter 22 has been positioned properly, the wire 24 may be withdrawn and, as this is done, the slits 26 resiliently re-close the aperture 25 to the restricted condition shown in Figure 6.

Another feature of the catheter 22 is that it has side holes

27, a plurality of which are provided very closely adjacent the tip aperture 25. In the example shown, there are three side apertures 27 spaced around the circumference of the catheter very close to the tip, for example within 5mm of the tip for a catheter used for coronary angiography.

Alternative configurations are shown in Figures 8 to 10.

As has been referred to above, certain open ended catheters of the type shown in Figure 1 have a "soft tip" made of elastic material as opposed to the firm material used in the main core of the body of the catheter. In the catheter shown in Figures 8 to 10, which is generally indicated at 28, a firm core 29 is surrounded by a coating of suitably elastic material 30 such as latex or silicone rubber which extends at the tip to form a resilient peripheral restrictor 31, restricting the aperture 40 at the tip by reducing the normal internal diameter of the catheter lumen 32 to a closed or virtually closed condition under normal circumstances. This restricted configuration is as illustrated in Figure 8. The peripheral restrictor 31 is annular in shape (Figure 8B) although it could possibly comprise a number of inwardly directed relatively localised restrictor members 33 which tend to partly close up the aperture 40 in the normal restricted condition as illustrated in Figure 8A.

Figure 9 shows the catheter 28 of Figure 8 with a guide wire 34 deployed. The aperture 40 defined by the peripheral restrictor 31 has been resiliently opened so that the terminal aperture 40 adopts an enlarged wire carrying configuration. The internal diameter of the lumen 32 may conform very closely to the external diameter of the wire 34 but preferably provides a small clearance as shown. This means that the resilient peripheral restrictor 31 is a snug fit around the wire.

In use, the device is illustrated in Figure 10. The catheter 28 is shown positioned within an artery whose wall is indicated at 35. It will be seen that the artery 35 is bifurcated into a main branch 36 and a small side branch 37 in this example. This figure will illustrate more clearly the effectiveness of the present invention.

As before in relation to Figures 5 to 7, the catheter of Figures 8 to 10 has a plurality of side holes 38, again peripherally spaced around the catheter and close to the extreme tip and its terminal aperture. Once the catheter has been positioned and the guide wire 34 removed, an injection of radio-opaque contrast medium can be carried out to provide visualisation of the artery at the position of the tip 40. In the case of a catheter having an end hole only such as that illustrated in Figure 1, the contrast medium issues linearly and forcefully from the tip aperture 11 and would provide adequate visualisation of the main branch 36. However because the tip of the catheter is positioned slightly beyond the small side branch 37 of the bifurcated artery, no visualisation of this side branch would take place. Further, the central forceable jet of medium issuing along the main branch 36 might not pick up areas of disease on the arterial walls very satisfactorily.

However by the use of the peripheral side holes 38 provided in the catheter of the present invention, together with the restricted tip aperture 40, a "spray" effect is achieved with the contrast medium which spreads out into both the main artery 36 and the small side branch 37, tending to billow and cling to the walls and highlight the contours in a very advantageous way.

The terminal aperture 40 at the tip 39 will be in its restricted configuration and may be closed or almost closed during injection. However it may be helpful if some portion

of the injected medium emanates from the tip aperture as well as through the side holes 38 since this gives the best pattern of contrast medium.

Because the injected medium is diffused, passing out through various different holes 38, 40, at the side and end of the catheter tip 39, there is less danger due to the forceful injection of contrast medium. Such danger may arise using prior art catheters because of the risk of damage to the arterial wall, disruption or removal of plaque from a diseased portion of the arterial wall or arrythmia.

Further and surprisingly, it has been found that the use of a catheter having side holes greatly reduces the amount of recoil of the catheter on injection with contrast medium. It will be appreciated that when the contrast medium emerges from the end hole 11 of the Figure 1 form of catheter, a reaction force is exerted on the catheter tending to push it out of position, which may make it difficult for the physician to continue observation of the artery.

The surprising lack of recoil in the clinical tests carried out using the device of the present invention is an important advantage.

Clinical tests have been carried out, principally using the modified form of Judkins catheter shown in Figures 5 to 7 of the drawings and its right handed counterpart. The clinical experience to date indicates the following points.

The invention is used in exactly the same way as the existing catheter of the same type so no new techniques need to be learned by the physician. It can be positioned using a guide wire.

The procedure time is shortened. Repeated imaging is not

necessary because the "spray effect" of the contrast medium from the catheter provides much better images.

The positional stability of the catheter is greatly improved during forced injection of contrast medium. There is little or no recoil detectable.

In difficult cases, imaging of proximal bifurcations is achievable. For example where the patient has a short left main stem the conventional end hole only catheter may lodge primarily in the left anterior descending artery, giving rise to poor or even no imaging of the circumflex artery for example.

Despite the presence of proximal disease, the catheter tip does not cause disruption of plaque. This is again due to the relative spreading of the contrast medium on injection.

Where tip engagement takes place into a small branch, typically in the right coronary artery, a conventional catheter as shown in Figure 1 would normally be expected to cause a fall in the pressure as monitored via the catheter, arrythmia when unintentional pressure injection is applied and a lack of contrast in the main artery. To date, none of the above difficulties have been observed with the prototype device even when the tip was engaged in a small branch.

Although clinical experience to the present date has been confined principally to use of catheters for angiography, it is believed that suitably sized catheters may be very useful for interventional cardiology for example percutaneous transluminal coronary angioplasty (PTCA). In balloon angioplasty, a guiding catheter is positioned using a guide wire. The guide catheter is left in position and a small balloon catheter is fed through it so that the balloon can be positioned within a constricted portion of artery, where it is

inflated to expand the lumen of the artery. Guide catheters used for PTCA are usually soft tip catheters having an end hole only. The soft tip is useful because of the slightly larger size of the catheters, and the need to avoid damage not merely to the patients tissue but also to the very delicate balloon catheter as it is passed.

Although a guide catheter has been available in which two or three side holes have been provided some 3cm to 4 cm from the tip, this is only to allow perfusion and pressure measurement to continue where the tip of the catheter occludes a small artery. Contrast injection is hampered in such available catheters because the contrast medium escapes too far away from the target site.

It is envisaged that using a catheter having the features of the present invention, namely side holes close to the tip and a self-closing or self-restricting tip aperture, substantial advantages can be gained. Firstly, the manoeuvring of the guide catheter can be safely achieved due to the capability of using a guide wire. The wire can be removed and the balloon catheter passed without any alteration in the standard techniques currently adopted. However the imaging available would be considerably better for the reasons outlined above in connection with angiography. Provided that the peripheral restrictor or tip construction is sufficiently compliant, the passage of the balloon catheter would be unimpeded with possibly some slight increase in resistance.

During PTCA, while the balloon is in the vessel, repeated angiography is necessary to monitor the progress of expanding the occluded lumen. Conventional guide catheters use the same end hole through which the balloon catheter is deployed. Since the balloon catheter reduces the size of the end hole of a conventional catheter, contrast injections are not always as successful in visualising the target vessel and surrounding

vessels as might be desired. Also the catheter is often deep in the target vessel and the contrast medium may not fill other important branches which the operator may wish to visualise.

It is believed that the form of resilient peripheral restrictor which is annular in shape as illustrated in Figure 8B may provide the best arrangement for a PTCA guide catheter rather than the form shown in Figure 8A or the slit type arrangement shown in Figure 6A. This is because the type of arrangement shown in Figure 6A would tend to lose its rounded tip, for example as shown in the deployed condition in Figure 7, when the PTCA device is in position but the resilient peripheral restrictor of Figure 8 would retain a smooth outer and inner contour. The catheter could be used for other interventional procedures for example insertion of stents.

Catheter devices as set out in the claims of this application may be adapted for use in other circumstances such as for example neuro-radiology or peripheral arterial work.

CLAIMS

1. A catheter comprising a hollow lumen having a distal end provided with a tip for insertion into a blood vessel, a plurality of peripherally spaced holes closely adjacent the tip, the tip having a terminal aperture capable of adopting two configurations, namely an enlarged wire carrying configuration in which it is capable of receiving and passing a wire, and a restricted configuration in which it is of substantially smaller cross-sectional area than in the enlarged condition, the aperture being normally biased into said restricted configuration.

2. A catheter according to claim 1 wherein said aperture comprises a slit.

3. A catheter according to claim 2 wherein said aperture comprises a plurality of intersecting slits.

4. A catheter according to claim 1 wherein said aperture is provided with a resilient peripheral restrictor.

5. A catheter according to claim 4 wherein the resilient peripheral restrictor comprises an annulus of resilient material surrounding and at least partly closing the aperture in the restricted configuration.

6. A catheter according to claim 4 wherein the resilient peripheral restrictor comprises a plurality of inwardly projecting restrictor members of resilient material which at least partly closed the aperture in the restricted configuration.

7. A catheter according to any one of claims 4 to 6 wherein the resilient material of the resilient peripheral restrictor is latex.

8. A catheter according to any one of claims 4 to 6 wherein the resilient material of the resilient peripheral restrictor is silicone rubber.

9. A catheter according to any one of claims 4 to 8 wherein the catheter is externally coated with a material which also forms the resilient peripheral restrictor.

10. A catheter according to claim wherein the aperture comprises a self-closing valve operable by a wire to open it into an enlarged configuration.

11. A catheter according to any preceding claim and adapted for use in diagnostic angiography.

12. A catheter according to any one of claims 1 to 11 and adapted for use as a guide catheter for cardiac interventional procedures.

13. A catheter substantially as hereinbefore described with reference to and as illustrated in Figures 5 to 7 of the accompanying drawings.

14. A catheter substantially as hereinbefore described with reference to and as illustrated in Figures 8 to 10 of the accompanying drawings.

Fig. 1

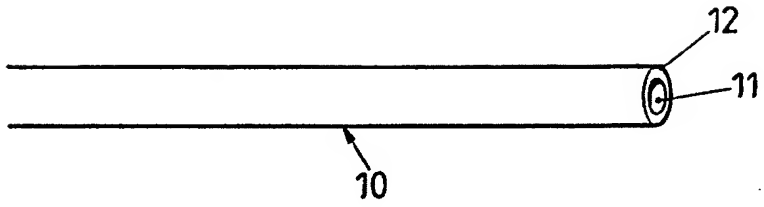


Fig. 2

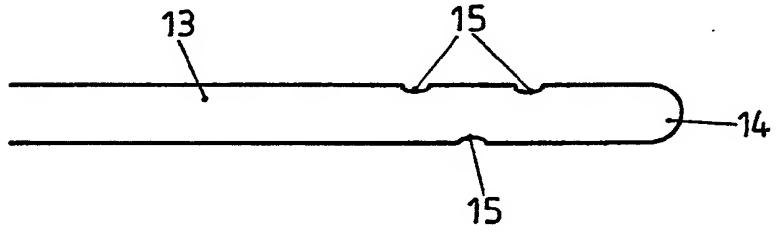


Fig. 3a

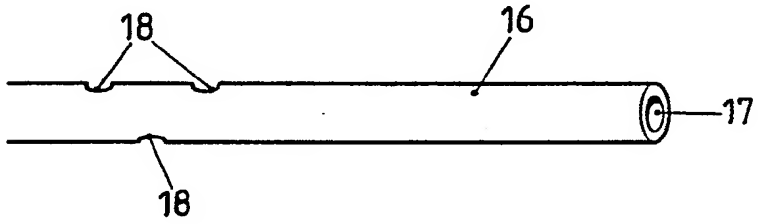


Fig. 3b

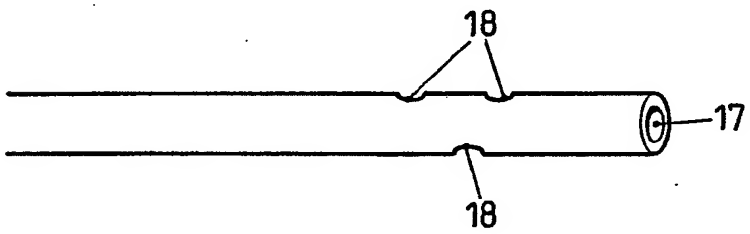


Fig. 4

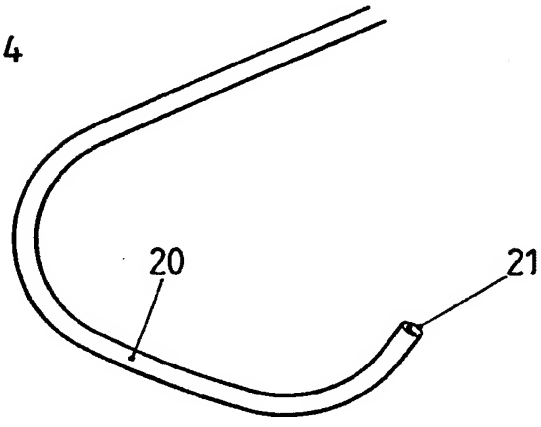


Fig.5

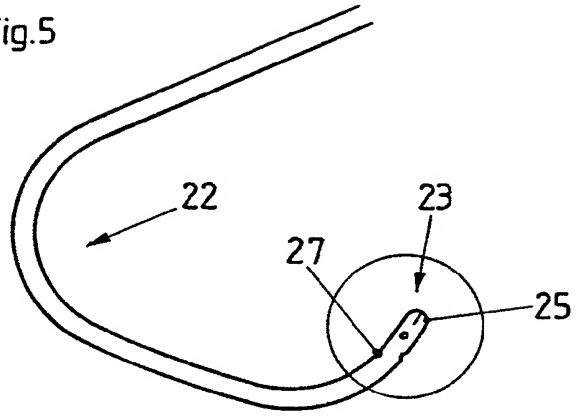
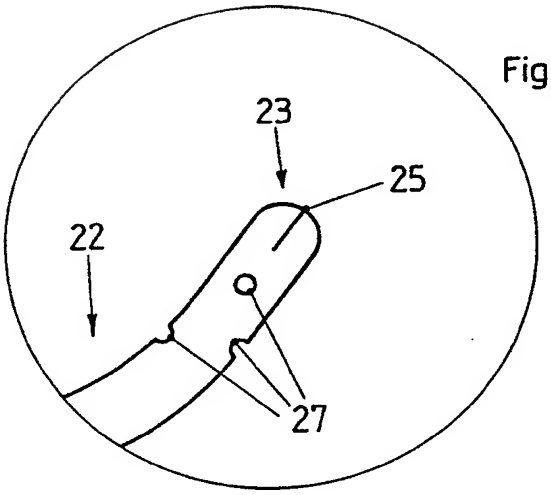


Fig.6



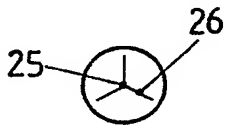


Fig.6a

Fig.7

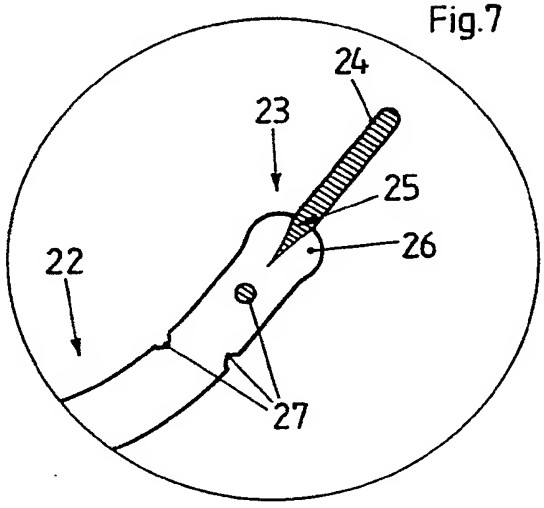


Fig.8

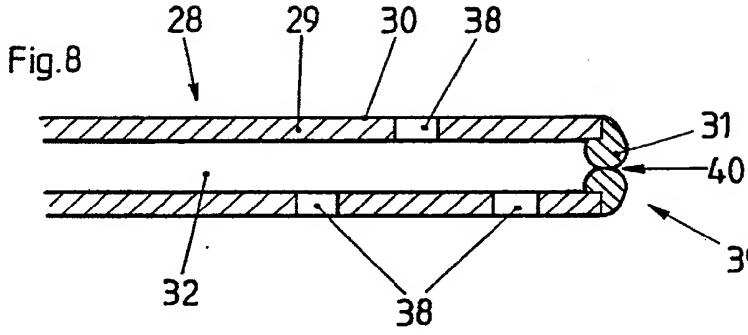


Fig.8a

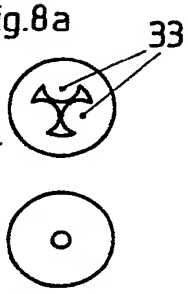


Fig.8b

Fig.9

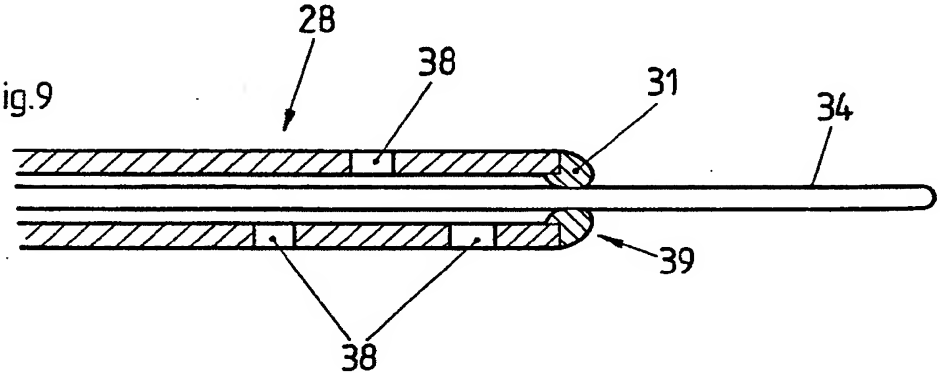
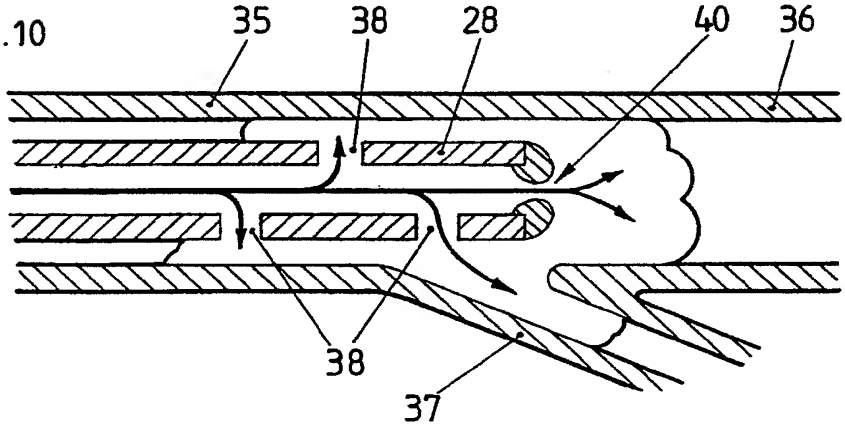


Fig.10



INTERNATIONAL SEARCH REPORT

Inter. ional Application No
PCT/GB 94/01841

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61M25/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61M A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US,A,4 023 559 (GASKELL) 17 May 1977 * THE WHOLE DOCUMENT *	1-10
Y	US,A,5 085 635 (CRAGG) 4 February 1992 see abstract; claims 1-4; figures 1,2	1-3,10
Y,P	WO,A,93 25263 (CARDIAC PATHWAYS CORPORATION) 23 December 1993 see page 7, line 19 - line 26; figures 2,4	1,4-9
A	WO,A,89 01352 (TARGET THERAPEUTICS) 23 February 1989 see abstract; claims 1,3; figures 2-4	1,4-9, 11,12
A	US,A,5 035 705 (BURNS) 30 July 1991 see abstract; figures 1-5	1,4-9

☐ Further documents are listed in the continuation of box C.

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Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Michels, N

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. ..onal Application No
PCT/GB 94/01841

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US-A-4023559	17-05-77	AU-B-	497345	07-12-78
		AU-A-	1039676	28-07-77
US-A-5085635	04-02-92	NONE		
WO-A-9325263	23-12-93	US-A-	5236424	17-08-93
WO-A-8901352	23-02-89	US-A-	4813934	21-03-89
		AU-A-	2307488	09-03-89
		CA-A-	1326423	25-01-94
		DE-D-	3884954	18-11-93
		DE-T-	3884954	03-02-94
		EP-A,B	0368931	23-05-90
		JP-T-	3502051	16-05-91
		JP-B-	4017667	26-03-92
		US-A-	5135494	04-08-92
US-A-5035705	30-07-91	US-A-	5085636	04-02-92
		US-A-	5221260	22-06-93